

WHAT IS CLAIMED IS:

1. A method for the prophylaxis or treatment of a pathological condition, the method comprising administering to a subject susceptible to or afflicted with such condition an aldosterone receptor antagonist and a neutral endopeptidase inhibitor, for the prophylaxis or treatment of the pathological condition.
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2. The method of claim 1 wherein the aldosterone receptor antagonist and neutral endopeptidase inhibitor are simultaneously provided to the subject as part of a single composition.
3. The method of claim 1 wherein a first amount of the aldosterone receptor antagonist and a second amount of the neutral endopeptidase inhibitor are provided to the subject in sequence as part of a timed relationship.
4. The method of claim 1 wherein the pathological condition is selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease,
5 retinopathy, neuropathy, insulinopathy, edema, endothelial dysfunction, and baroreceptor dysfunction.
5. The method of claim 4,
wherein the cardiovascular disease is selected from the group consisting of heart failure, arrhythmia, diastolic dysfunction, systolic dysfunction, ischemia, hypertrophic
5 cardiomyopathy, sudden cardiac death, myocardial fibrosis, vascular fibrosis, impaired arterial compliance, myocardial necrotic lesions, vascular damage, myocardial infarction, left ventricular hypertrophy, decreased ejection fraction, cardiac lesions, vascular wall hypertrophy, endothelial thickening,
10 and fibrinoid necrosis of coronary arteries;

wherein the renal dysfunction is selected from the group consisting of glomerulosclerosis, end-stage renal disease, diabetic nephropathy, reduced renal blood flow, increased glomerular filtration fraction, proteinuria, decreased
15 glomerular filtration rate, decreased creatinine clearance, microalbuminuria, renal arteriopathy, ischemic lesions, thrombotic lesions, global fibrinoid necrosis, focal thrombosis of glomerular capillaries, swelling and proliferation of intracapillary cells, swelling and
20 proliferation of extracapillary cells, expansion of reticulated mesangial matrix with or without significant hypercellularity, and malignant nephrosclerosis;

wherein the liver disease is selected from the group consisting of liver cirrhosis, liver ascites, and hepatic
25 congestion;

wherein the cerebrovascular disease is stroke;

wherein the vascular disease is selected from the group consisting of thrombotic vascular disease, proliferative arteriopathy, atherosclerosis, decreased vascular compliance,
30 and endothelial dysfunction;

wherein the insulinopathy is selected from the group consisting of insulin resistance, Type I diabetes mellitus, Type II diabetes mellitus, glucose resistance, pre-diabetic state, and syndrome X; and

35 wherein the edema is selected from the group consisting of peripheral tissue edema, hepatic congestion, splenic congestion, liver ascites, respiratory congestion, and lung congestion.

6. The method of claim 1 wherein the aldosterone receptor antagonist is an epoxy-steroidal-type compound characterized in having a 9 α -, 11 α -substituted epoxy moiety.

7. The method of claim 1 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

8. The method of claim 1 wherein the aldosterone receptor antagonist is selected from the group consisting of:

pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo, γ -lactone, methyl ester, (7 α ,11 α ,17 α) - ;

5 pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, (7 α ,11 α ,17 α) - ;

3'H-cyclopropano(6,7) prena-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 β ,17 β) - ;

10 pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) - ;

15 pregn-4-ene-7,21-dicarboxylic acid, 9,11,-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α ,17 α) - ;

3'H-cyclopropano(6,7) prena-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -actone (6 α ,7 α ,11 α) - ;

20 3'H-cyclopropano(6,7) prena-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6 α ,7 α ,11 α ,17 α) - ;

3'H-cyclopropano(6,7) prena-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, (6 α ,7 α ,11 α ,17 α) - ;

25 3'H-cyclopropano(6,7)pregna-4,6-diene-21-carboxylic acid,
9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone,
(6 α ,7 α ,11 α ,17 α) - ;

pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-
hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 α) - ; and

30 pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-
hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester,
(7 α ,11 α ,17 α) - .

9. The method of claim 1 wherein the neutral
endopeptidase inhibitor is selected from the group consisting
of candoxatril, candoxatrilat, ecadotril, phosphoramidon, and
the pharmaceutically acceptable salts, esters, conjugate
5 acids, and prodrugs thereof.

10. The method of claim 1 wherein the aldosterone
receptor antagonist is administered in a daily dose ranging
from about 0.1 to 2000 mg, and the neutral endopeptidase
inhibitor is administered in a daily dose ranging from about
5 0.1 to 1000 mg.

11. The method of claim 1 wherein the first amount of
the aldosterone receptor antagonist produces no substantial
diuretic or anti-hypertensive effect in a subject.

12. The method of claim 1 further comprising
administering a third amount of a compound selected from the
group consisting of renin inhibitors, angiotensin I
antagonists, angiotensin II antagonists, angiotensin
5 converting enzyme inhibitors, alpha-adrenergic receptor
blockers, beta-adrenergic receptor blockers, calcium channel
blockers, endothelin receptor antagonists, endothelin
converting enzymes, vasodilators, diuretics, cyclooxygenase-2
inhibitors, apical sodium bile acid transport inhibitors,
10 cholesterol absorption inhibitors, fibrates, niacin, statins,

cholesteryl ester transfer protein inhibitors, bile acid sequestrants, anti-oxidants, vitamin E, probucol, and IIb/IIIa antagonists.

13. The method of claim 1 further comprising administering a third amount of an angiotensin converting enzyme inhibitor.

14. The method of claim 13 wherein the angiotensin converting enzyme inhibitor is selected from the group consisting of benazapril, captopril, cilazapril, enalapril, fosinopril, lisinopril, perindopril, quinopril, ramipril,
5 trandolapril, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

15. The method of claim 13 wherein the aldosterone receptor antagonist is administered in a daily dose ranging from about 0.1 to 2000 mg, the neutral endopeptidase inhibitor is administered in a daily dose ranging from about 0.1 to 1000
5 mg, and the angiotensin converting enzyme inhibitor is administered in a daily dose ranging from about 0.1 to 1000 mg.

16. The method of claim 13 wherein the first amount of the aldosterone receptor antagonist produces no substantial diuretic or anti-hypertensive effect in a subject.

17. A combination comprising an aldosterone receptor antagonist and a neutral endopeptidase inhibitor in a pharmaceutically acceptable carrier.

18. The combination of claim 17 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

19. A method for the prophylaxis or treatment of a pathological condition, the method comprising administering to

a subject susceptible to or afflicted with such condition an aldosterone receptor antagonist and a vasopeptidase inhibitor other than omapatrilat, for the prophylaxis or treatment of a pathological condition.

20. The method of claim 19 wherein the aldosterone receptor antagonist and vasopeptidase inhibitor are simultaneously provided to the subject as part of a single composition.

21. The method of claim 19 wherein a first amount of the aldosterone receptor antagonist and a second amount of the vasopeptidase inhibitor are provided to the subject in sequence as part of a timed relationship.

22. The method of claim 19 wherein the pathological condition is selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease, retinopathy, neuropathy, insulinopathy, edema, endothelial dysfunction, and baroreceptor dysfunction.

23. The method of claim 22,

wherein the cardiovascular disease is selected from the group consisting of heart failure, arrhythmia, diastolic dysfunction, systolic dysfunction, ischemia, hypertrophic cardiomyopathy, sudden cardiac death, myocardial fibrosis, vascular fibrosis, impaired arterial compliance, myocardial necrotic lesions, vascular damage, myocardial infarction, left ventricular hypertrophy, decreased ejection fraction, cardiac lesions, vascular wall hypertrophy, endothelial thickening, and fibrinoid necrosis of coronary arteries;

wherein the renal dysfunction is selected from the group consisting of glomerulosclerosis, end-stage renal disease, diabetic nephropathy, reduced renal blood flow, increased

15 glomerular filtration fraction, proteinuria, decreased
glomerular filtration rate, decreased creatinine clearance,
microalbuminuria, renal arteriopathy, ischemic lesions,
thrombotic lesions, global fibrinoid necrosis, focal
thrombosis of glomerular capillaries, swelling and
proliferation of intracapillary cells, swelling and
20 proliferation of extracapillary cells, expansion of
reticulated mesangial matrix with or without significant
hypercellularity, and malignant nephrosclerosis;

25 wherein the liver disease is selected from the group
consisting of liver cirrhosis, liver ascites, and hepatic
congestion;

wherein the cerebrovascular disease is stroke;

30 wherein the vascular disease is selected from the group
consisting of thrombotic vascular disease, proliferative
arteriopathy, atherosclerosis, decreased vascular compliance,
and endothelial dysfunction;

wherein the insulinopathy is selected from the group
consisting of insulin resistance, Type I diabetes mellitus,
Type II diabetes mellitus, glucose resistance, pre-diabetic
state, and syndrome X; and

35 wherein the edema is selected from the group consisting
of peripheral tissue edema, hepatic congestion, splenic
congestion, liver ascites, respiratory congestion, and lung
congestion.

24. The method of claim 19 wherein the aldosterone
receptor antagonist is an epoxy-steroidal-type compound
characterized in having a 9 α -, 11 α -substituted epoxy moiety.

25. The method of claim 19 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

26. The method of claim 19 wherein the aldosterone receptor antagonist is a spirolactone-type compound.

27. The method of claim 19 wherein the aldosterone receptor antagonist is selected from the group consisting of:

pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo, γ -lactone, methyl ester, (7 α ,11 α ,17 α) -;

5 pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, (7 α ,11 α ,17 α) -;

3'H-cyclopropano(6,7) pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 β ,17 β) -;

10 pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) -;

15 pregn-4-ene-7,21-dicarboxylic acid, 9,11,-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α ,17 α) -;

3'H-cyclopropano(6,7)pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, g-actone(6 α ,7 α ,11 α) -;

20 3'H-cyclopropano(6,7)pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6 α ,7 α ,11 α ,17 α) -;

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3'H-cyclopropa(6,7)pregna-4,6-diene-21-carboxylic acid,
9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium
salt, (6 α ,7 α ,11 α ,17 α) - ;

25 3'H-cyclopropa(6,7)pregna-4,6-diene-21-carboxylic acid,
9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone,
(6 α ,7 α ,11 α ,17 α) - ;

pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-
hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 α) - ; and

30 pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-
hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester,
(7 α ,11 α ,17 α) - .

28. The method of claim 55 wherein the vasopeptidase
inhibitor is selected from the group consisting of
gemopatrilat, sampatrilat, fasidotril, racecadotril, GW660511,
M100240, and the pharmaceutically acceptable salts, esters,
5 conjugate acids, and prodrugs thereof.

29. The method of claim 19 wherein the aldosterone
receptor antagonist is administered in a daily dose ranging
from about 0.1 to 2000 mg, and the vasopeptidase inhibitor is
administered in a daily dose ranging from about 0.1 to 1000
5 mg.

30. The method of claim 19 wherein the first amount of
the aldosterone receptor antagonist produces no substantial
diuretic or anti-hypertensive effect in a subject.

31. The method of claim 19 further comprising
administering a third amount of a compound selected from the
group consisting of renin inhibitors, angiotensin I
antagonists, angiotensin II antagonists, angiotensin
5 converting enzyme inhibitors, alpha-adrenergic receptor
blockers, beta-adrenergic receptor blockers, calcium channel

blockers, endothelin receptor antagonists, endothelin converting enzymes, vasodilators, diuretics, cyclooxygenase-2 inhibitors, apical sodium bile acid transport inhibitors,
10 cholesterol absorption inhibitors, fibrates, niacin, statins, cholestryl ester transfer protein inhibitors, bile acid sequestrants, anti-oxidants, vitamin E, probucol, and IIb/IIIa antagonists.

32. The method of claim 19 further comprising administering a third amount of an angiotensin converting enzyme inhibitor.

33. The method of claim 32 wherein the angiotensin converting enzyme inhibitor is selected from the group consisting of benazapril, captopril, cilazapril, enalapril, fosinopril, lisinopril, perindopril, quinopril, ramipril,
5 trandolapril, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

34. The method of claim 32 wherein the aldosterone receptor antagonist is administered in a daily dose ranging from about 0.1 to 2000 mg, the vasopeptidase inhibitor is administered in a daily dose ranging from about 0.1 to 1000
5 mg, and the angiotensin converting enzyme inhibitor is administered in a daily dose ranging from about 0.1 to 1000 mg.

35. The method of claim 32 wherein the first amount of the aldosterone receptor antagonist produces no substantial diuretic or anti-hypertensive effect in a subject.

36. A combination comprising an aldosterone receptor antagonist and a vasopeptidase inhibitor, other than omapatrilat, in a pharmaceutically acceptable carrier.

37. The combination of claim 36 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

38. A method for the prophylaxis or treatment of a pathological condition, the method comprising administering to a subject susceptible to or afflicted with such condition an aldosterone receptor antagonist and a vasopeptidase inhibitor
5 for the prophylaxis or treatment of a pathological condition,

wherein the aldosterone receptor antagonist exhibits a release profile, determined using a suitable release profile test, in which more than about 20% by weight of the aldosterone receptor antagonist is released within about four
10 hours after initiation of the test.

39. The method of claim 38 wherein the aldosterone receptor antagonist and vasopeptidase inhibitor are simultaneously provided to the subject as part of a single composition.

40. The method of claim 38 wherein a first amount of the aldosterone receptor antagonist and a second amount of the vasopeptidase inhibitor are provided to the subject in sequence as part of a timed relationship.

41. The method of claim 38 wherein the pathological condition is selected from the group consisting of hypertension, cardiovascular disease, renal dysfunction, liver disease, cerebrovascular disease, vascular disease,
5 retinopathy, neuropathy, insulinopathy, edema, endothelial dysfunction, and baroreceptor dysfunction.

42. The method of claim 38,

wherein the cardiovascular disease is selected from the group consisting of heart failure, arrhythmia, diastolic

dysfunction, systolic dysfunction, ischemia, hypertrophic
5 cardiomyopathy, sudden cardiac death, myocardial fibrosis,
vascular fibrosis, impaired arterial compliance, myocardial
necrotic lesions, vascular damage, myocardial infarction, left
ventricular hypertrophy, decreased ejection fraction, cardiac
lesions, vascular wall hypertrophy, endothelial thickening,
10 and fibrinoid necrosis of coronary arteries;

wherein the renal dysfunction is selected from the group
consisting of glomerulosclerosis, end-stage renal disease,
diabetic nephropathy, reduced renal blood flow, increased
15 glomerular filtration fraction, proteinuria, decreased
glomerular filtration rate, decreased creatinine clearance,
microalbuminuria, renal arteriopathy, ischemic lesions,
thrombotic lesions, global fibrinoid necrosis, focal
thrombosis of glomerular capillaries, swelling and
proliferation of intracapillary cells, swelling and
20 proliferation of extracapillary cells, expansion of
reticulated mesangial matrix with or without significant
hypercellularity, and malignant nephrosclerosis;

wherein the liver disease is selected from the group
consisting of liver cirrhosis, liver ascites, and hepatic
25 congestion;

wherein the cerebrovascular disease is stroke;

wherein the vascular disease is selected from the group
consisting of thrombotic vascular disease, proliferative
arteriopathy, atherosclerosis, decreased vascular compliance,
30 and endothelial dysfunction;

wherein the insulinopathy is selected from the group
consisting of insulin resistance, Type I diabetes mellitus,
Type II diabetes mellitus, glucose resistance, pre-diabetic
state, and syndrome X; and

35 wherein the edema is selected from the group consisting of peripheral tissue edema, hepatic congestion, splenic congestion, liver ascites, respiratory congestion, and lung congestion.

43. The method of claim 38 wherein the aldosterone receptor antagonist is an epoxy-steroidal-type compound characterized in having a 9 α -, 11 α -substituted epoxy moiety.

44. The method of claim 38 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

45. The method of claim 38 wherein the aldosterone receptor antagonist is a spirolactone-type compound.

46. The method of claim 38 wherein the aldosterone receptor antagonist is selected from the group consisting of:

pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo, γ -lactone, methyl ester, (7 α ,11 α ,17 α) - ;

5 pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, (7 α ,11 α ,17 α) - ;

3'H-cyclopropa(6,7) prena-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 β ,17 β) - ;

10 pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 α) - ;

15 pregn-4-ene-7,21-dicarboxylic acid, 9,11,-epoxy-17-hydroxy-3-oxo-,7-methyl ester, monopotassium salt, (7 α ,11 α ,17 α) - ;

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3'H-cyclopropa(6,7)pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, g-actone(6 α ,7 α ,11 α) -;

20 3'H-cyclopropa(6,7)pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6 α ,7 α ,11 α ,17 α) -;

3'H-cyclopropa(6,7)pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, (6 α ,7 α ,11 α ,17 α) -;

25 3'H-cyclopropa(6,7)pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 α ,7 α ,11 α ,17 α) -;

pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 α) -; and

30 pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, (7 α ,11 α ,17 α) -.

47. The method of claim 38 wherein the vasopeptidase inhibitor is selected from the group consisting of omapatrilat, gemopatrilat, sampatrilat, fasidotril, racecadotril, GW660511, M100240, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

48. The method of claim 38 wherein the aldosterone receptor antagonist is administered in a daily dose ranging from about 0.1 to 2000 mg, and the vasopeptidase inhibitor is administered in a daily dose ranging from about 0.1 to 1000 mg.

49. The method of claim 38 wherein the first amount of the aldosterone receptor antagonist produces no substantial diuretic or anti-hypertensive effect in a subject.

50. The method of claim 38 further comprising administering a third amount of a compound selected from the group consisting of renin inhibitors, angiotensin I antagonists, angiotensin II antagonists, angiotensin
5 converting enzyme inhibitors, alpha-adrenergic receptor blockers, beta-adrenergic receptor blockers, calcium channel blockers, endothelin receptor antagonists, endothelin converting enzymes, vasodilators, diuretics, cyclooxygenase-2 inhibitors, apical sodium bile acid transport inhibitors,
10 cholesterol absorption inhibitors, fibrates, niacin, statins, cholestryl ester transfer protein inhibitors, bile acid sequestrants, anti-oxidants, vitamin E, probucol, and IIb/IIIa antagonists.

51. The method of claim 38 further comprising administering a third amount of an angiotensin converting enzyme inhibitor.

52. The method of claim 51 wherein a first amount of the aldosterone receptor antagonist, a second amount of the
vasopeptidase inhibitor, and a third amount of the angiotensin
converting enzyme inhibitor are provided to the subject in
5 sequence as part of a timed relationship.

53. The method of claim 51 wherein the aldosterone receptor antagonist is administered in a daily dose ranging from about 0.1 to 2000 mg, the vasopeptidase inhibitor is administered in a daily dose ranging from about 0.1 to 1000
5 mg, and the angiotensin converting enzyme inhibitor is administered in a daily dose ranging from about 0.1 to 1000 mg.

54. The method of claim 51 wherein the first amount of the aldosterone receptor antagonist produces no substantial diuretic or anti-hypertensive effect in a subject.

55. A combination comprising an aldosterone receptor antagonist and a vasopeptidase inhibitor in a pharmaceutically acceptable carrier, wherein the aldosterone receptor antagonist exhibits a release profile, determined using a suitable release profile test, in which more than about 20% by weight of the aldosterone receptor antagonist is released within about four hours after initiation of the test.

56. The combination of claim 55 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

57. A pharmaceutical composition comprising a first amount of an aldosterone receptor antagonist, a second amount of a neutral endopeptidase inhibitor, and a pharmaceutically acceptable carrier.

58. The composition of claim 57 wherein the first amount of the aldosterone receptor antagonist and the second amount of the neutral endopeptidase inhibitor together comprise a therapeutically-effective amount of the aldosterone receptor antagonist and neutral endopeptidase inhibitor for the prophylaxis or treatment of a pathological condition.

59. The composition of claim 57 wherein the neutral endopeptidase inhibitor is selected from the group consisting of candoxatril, candoxatrilat, ecadotril, phosphoramidon, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

60. The composition of claim 57 wherein the first amount of the aldosterone receptor antagonist produces no substantial diuretic or anti-hypertensive effect in a subject.

61. The composition of claim 57 further comprising a third amount of a compound selected from the group consisting of renin inhibitors, angiotensin I antagonists, angiotensin II antagonists, angiotensin converting enzyme inhibitors, alpha-
5 adrenergic receptor blockers, beta-adrenergic receptor blockers, calcium channel blockers, endothelin receptor antagonists, endothelin converting enzymes, vasodilators, diuretics, cyclooxygenase-2 inhibitors, apical sodium bile acid transport inhibitors, cholesterol absorption inhibitors,
10 fibrates, niacin, statins, cholesteryl ester transfer protein inhibitors, bile acid sequestrants, anti-oxidants, vitamin E, probucol, and IIb/IIIa antagonists.

62. The composition of claim 57 further comprising administering a third amount of an angiotensin converting enzyme inhibitor.

63. The composition of claim 57 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

64. A pharmaceutical composition comprising a first amount of an aldosterone receptor antagonist, a second amount of a vasopeptidase inhibitor other than omapatrilat, and a pharmaceutically acceptable carrier.

65. The composition of claim 64 wherein the first amount of the aldosterone receptor antagonist and the second amount of the vasopeptidase inhibitor together comprise a therapeutically-effective amount of the aldosterone receptor antagonist and vasopeptidase inhibitor for the prophylaxis or
5 treatment of a pathological condition.

66. The composition of claim 64 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

67. The composition of claim 64 wherein the
vasopeptidase inhibitor is selected from the group consisting
of gemopatrilat, sampatrilat, fasidotril, racecadotril,
GW660511, M100240, and the pharmaceutically acceptable salts,
5 esters, conjugate acids, and prodrugs thereof.

68. The composition of claim 64 wherein the first amount
of the aldosterone receptor antagonist produces no substantial
diuretic or anti-hypertensive effect in a subject.

69. The composition of claim 64 further comprising a
third amount of a compound selected from the group consisting
of renin inhibitors, angiotensin I antagonists, angiotensin II
antagonists, angiotensin converting enzyme inhibitors, alpha-
5 adrenergic receptor blockers, beta-adrenergic receptor
blockers, calcium channel blockers, endothelin receptor
antagonists, endothelin converting enzymes, vasodilators,
diuretics, cyclooxygenase-2 inhibitors, apical sodium bile
acid transport inhibitors, cholesterol absorption inhibitors,
10 fibrates, niacin, statins, cholestryl ester transfer protein
inhibitors, bile acid sequestrants, anti-oxidants, vitamin E,
probucol, and IIb/IIIa antagonists.

70. The composition of claim 64 further comprising
administering a third amount of an angiotensin converting
enzyme inhibitor.

71. The composition of claim 70, wherein the angiotensin
converting enzyme inhibitor is selected from the group
consisting of benazapril, captopril, cilazapril, enalapril,
flosinopril, lisinopril, perindopril, quinopril, ramipril,
5 trandolapril, and the pharmaceutically acceptable salts,
esters, conjugate acids, and prodrugs thereof.

72. A pharmaceutical composition for the treatment or
prevention of a pathological condition comprising a first

amount of aldosterone receptor antagonist and a second amount of a vasopeptidase inhibitor,

5 wherein the first amount of the aldosterone receptor antagonist and the second amount of the vasopeptidase inhibitor together comprise a therapeutically-effective amount of the aldosterone receptor antagonist and vasopeptidase inhibitor for the prophylaxis or treatment of a pathological condition, and wherein said composition exhibits a release profile, determined using a suitable release profile test, in which more than about 20% by weight of the aldosterone receptor antagonist is released from the composition within about four hours after initiation of the test.

73. The composition of claim 72 wherein the first amount of the aldosterone receptor antagonist and the second amount of the vasopeptidase inhibitor together comprise a therapeutically-effective amount of the aldosterone receptor antagonist and vasopeptidase inhibitor for the prophylaxis or treatment of a pathological condition.

74. The composition of claim 72 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

75. The composition of claim 72 wherein the vasopeptidase inhibitor is selected from the group consisting of omapatrilat, gemopatrilat, sampatrilat, fasidotril, racecadotril, GW660511, M100240, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

76. The composition of claim 72 wherein the first amount of the aldosterone receptor antagonist produces no substantial diuretic or anti-hypertensive effect in a subject.

77. The composition of claim 72 further comprising a third amount of a compound selected from the group consisting of renin inhibitors, angiotensin I antagonists, angiotensin II antagonists, angiotensin converting enzyme inhibitors, alpha-
5 adrenergic receptor blockers, beta-adrenergic receptor blockers, calcium channel blockers, endothelin receptor antagonists, endothelin converting enzymes, vasodilators, diuretics, cyclooxygenase-2 inhibitors, apical sodium bile acid transport inhibitors, cholesterol absorption inhibitors,
10 fibrates, niacin, statins, cholesteryl ester transfer protein inhibitors, bile acid sequestrants, anti-oxidants, vitamin E, probucol, and IIb/IIIa antagonists.

78. The composition of claim 72 further comprising administering a third amount of an angiotensin converting enzyme inhibitor.

79. The composition of claim 78 wherein the angiotensin converting enzyme inhibitor is selected from the group consisting of benazapril, captopril, cilazapril, enalapril, fosinopril, lisinopril, perindopril, quinopril, ramipril,
5 trandolapril, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

80. A kit containing a first amount of an aldosterone receptor antagonist and a second amount of a neutral endopeptidase inhibitor.

81. The kit of claim 80 comprising the first amount of the aldosterone receptor antagonist in a unit dosage form, and the second amount of a neutral endopeptidase inhibitor in a unit dosage form.

82. The kit of claim 80 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

83. The kit of claim 80 wherein the neutral endopeptidase inhibitor is selected from the group consisting of candoxatril, candoxatrilat, ecadotril, phosphoramidon, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

84. The kit of claim 80 further comprising a third amount of an angiotensin converting enzyme inhibitor.

85. The kit of claim 84 wherein the angiotensin converting enzyme inhibitor is selected from the group consisting of benazapril, captopril, cilazapril, enalapril, fosinopril, lisinopril, perindopril, quinopril, ramipril, trandolapril, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

86. A kit containing a first amount of an aldosterone receptor antagonist and a second amount of a vasopeptidase inhibitor other than omapatrilat.

87. The kit of claim 86 comprising the first amount of the aldosterone receptor antagonist in a unit dosage form, and the second amount of a vasopeptidase inhibitor in a unit dosage form.

88. The kit of claim 86 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

89. The kit of claim 86 wherein the vasopeptidase inhibitor is selected from the group consisting of gemopatrilat, sampatrilat, fasidotril, racecadotril, GW660511, M100240, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

90. A kit containing a first amount of an aldosterone receptor antagonist and a second amount of a vasopeptidase

inhibitor, wherein the first amount of the aldosterone receptor antagonist exhibits a release profile, determined
5 using a suitable release profile test, in which more than about 20% by weight of the aldosterone receptor antagonist is released at about 4 hours after initiation of the test.

91. The kit of claim 90 comprising the first amount of the aldosterone receptor antagonist in a unit dosage form, and the second amount of a vasopeptidase inhibitor in a unit dosage form.

92. The kit of claim 90 wherein the aldosterone receptor antagonist is selected from the group consisting of eplerenone and spironolactone.

93. The kit of claim 90 wherein the vasopeptidase inhibitor is selected from the group consisting of omapatrilat, gemopatrilat, sampatrilat, fasidotril, racecadotril, GW660511, M100240, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

94. The kit of claim 90 further comprising a third amount of an angiotensin converting enzyme inhibitor.

95. The kit of claim 94 wherein the angiotensin converting enzyme inhibitor is selected from the group consisting of benazapril, captopril, cilazapril, enalapril, fosinopril, lisinopril, perindopril, quinopril, ramipril,
5 trandolapril, and the pharmaceutically acceptable salts, esters, conjugate acids, and prodrugs thereof.

96. The kit of claim 90 wherein at least about 30% by weight of the aldosterone receptor antagonist is released from the composition within about four hours after initiation of the test.